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EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 06/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/419,817	HUANG ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 23-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 23-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

FINAL ACTION

1. This action is in response to papers filed 8 April 2003 in which claims 1, 4-7, 23 and 26-29 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 9 December 2002 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1-16 and 23-38 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 2, 4, 6, 8-11, 13, 23, 24, 26, 28, 30-33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (WO 97/42345, published 13 November 1997) in view of Lane et al (U.S. Patent No. 6,165,714, filed 16 December 1997).

Regarding Claim 1, Whitcombe et al disclose a method to determine a nucleotide at a polymorphic locus in a nucleic acid sample (page 5, lines 11-30). The method comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (capture region) which is identical in sequence to all or part of a probe on a solid support (capture probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to al or part of the probe; labeling the amplified DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support wherein the presence of said labeled amplified DNA products on the solid support indicates that the nucleic acid sample contains at the polymorphic locus a nucleotide which is the same as the 3' terminal nucleotide of the primer (page 1, line 28-page 3, line 6; page 14, lines 1-15; Fig. 13(b) and Claims 1 & 8). The first primer of Whitcombe et al comprises a capture region and terminates at the 5' end with a tag sequence for identification of the amplified product (page 14, lines 6-9) but they do not teach the first primer terminates at the 5 'end with the capture region. However, Lane et al teach the similar method wherein a region of DNA is amplified using a primer pair wherein the first primer terminates at the 5' end with a portion which is identical to the probe on the solid support (Column 8, lines 36-40 and Fig. 9B #80). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tag-comprising primer of Whitcombe et al by terminating the primer at the 5' end with the capture sequence as taught by Lane et al to thereby simplify primer design by elimination of the tag

sequence. Lane et al teach that the extension product is detected upon capture (Column 8, lines 23-41). Therefore, the tag sequence of Whitcombe et al is not required for extension product detection. Hence, one of ordinary skill in the art would have been motivated to eliminate the tag sequence of the Whitcombe et al primer based on the teaching of Lane et al wherein the tag sequence is not required for product detection.

The courts have stated that it would be obvious to omit an element when a function attributed to said element is not desired or required (see Ex parte Wu, 10 USPQ 2031).

Regarding Claim 2, Whitcombe et al disclose the method wherein the step of labeling couples a labeled nucleotide to a 3' end i.e. labeled NTPs are incorporated into the primer extension products by coupling to the 3' end during primer extension (page 3, lines 5-6).

Regarding Claim 4, Whitcombe et al disclose the method wherein the nucleotide is fluorescently labeled (page 2, lines 23-31 and Claim 5).

Regarding Claim 6, Whitcombe et al disclose the method wherein the nucleotide is enzymatically labeled (page 14, lines 10-15 and Fig. 13(b)).

Regarding Claim 8, Whitcombe et al disclose the method further comprising optically detecting fluorescent label on the solid support (page 2, line 23-page 3, line 3).

Regarding Claim 9, Whitcombe et al disclose the method wherein two primer pairs are employed wherein the first primer of each of the first and second pairs of primers terminate at their 3' ends in distinct nucleotides and wherein each 5' portion of each of said first primers is identical in sequence to all or part of a distinct probe (page 7, lines 6-24 and Claim 15) and wherein the probe is at a known location on a solid support i.e. the capture probe is immobilized on a solid support wherein the known location is on the solid support (page 2, line 31-page 3, line 2 and Claim 8).

Regarding Claim 10, Whitcombe et al disclose the method wherein quantities of fluorescent label at known locations on the solid support are compared wherein the known locations represent different allelic forms of the polymorphic locus having difference

nucleotides at the polymorphic locus thereby determining a ratio of nucleotides at the polymorphic locus in the sample (page 11, lines 8-12 and Fig. 5).

Regarding Claim 11, Whitcombe et al disclose the method wherein the ratio of nucleotides at two or more polymorphic loci are determined simultaneously i.e. multiplex (page 8, lines 7-9).

Regarding Claim 13, Whitcombe et al disclose the method wherein two or more regions of DNA each of which comprise a polymorphic locus are amplified in a single reaction mixture (page 7, lines 11-15).

Regarding Claim 23, Whitcombe et al disclose a method to prepare samples for analysis to determine a nucleotide at a polymorphic locus in a nucleic acid sample (page 5, lines 11-30). The method comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA products using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (tag region) which is identical in sequence to all or part of a probe on a solid support (capture probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to all or part of the probe; labeling the amplified DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridizes to the probe on the solid support thereby forming prepared samples for analysis (page 1, line 28-page 3, line 6, Fig. 13(b) and Claims 1 & 8). The first primer of Whitcombe et al comprises a capture region and terminates at the 5' end with a tag sequence for identification of the amplified product (page 14, lines 6-9) but they do not teach the first primer terminates at the 5 'end with the capture region. However, Lane et al teach the similar method wherein a region of DNA is amplified using a primer pair wherein the first

primer terminates at the 5' end with a portion which is identical to the probe on the solid support (Column 8, lines 36-40 and Fig. 9B #80). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tag-comprising primer of Whitcombe et al by terminating the primer at the 5' end with the capture sequence as taught by Lane et al to thereby simplify primer design by elimination of the tag sequence. Lane et al teach that the extension product is detected upon capture (Column 8, lines 23-41). Therefore, the tag sequence of Whitcombe et al is not required for extension product detection. Hence, one of ordinary skill in the art would have been motivated to eliminate the tag sequence of the Whitcombe et al primer based on the teaching of Lane et al wherein the tag sequence is not required for product detection.

Regarding Claim 24, Whitcombe et al disclose the method wherein the step of labeling couples a labeled nucleotide to a 3' end i.e. labeled NTPs are incorporated into the primer extension products by coupling to the 3' end during primer extension (page 3, lines 5-6).

Regarding Claim 26, Whitcombe et al disclose the method wherein the nucleotide is fluorescently labeled (page 2, lines 23-31 and Claim 5).

Regarding Claim 28, Whitcombe et al disclose the method wherein the nucleotide is enzymatically labeled (page 14, lines 10-15 and Fig. 13(b)).

Regarding Claim 30, Whitcombe et al disclose the method further comprising optically detecting fluorescent label on the solid support (page 2, line 23-page 3, line 3).

Regarding Claim 31, Whitcombe et al disclose the method wherein two primer pairs are employed wherein the first primer of each of the first and second pairs of primers terminate at their 3' ends in distinct nucleotides and wherein each 5' portion of each of said first primers is identical in sequence to all or part of a distinct probe (page 7, lines 6-24 and Claim 15) and wherein the probe is at a known location on a solid support i.e. the capture probe is immobilized on a solid support wherein the known location is on the solid support (page 2, line 31-page 3, line 2 and Claim 8).

Regarding Claim 32, Whitcombe et al disclose the method wherein quantities of fluorescent label at known locations on the solid support are compared wherein the known locations represent different allelic forms of the polymorphic locus having difference nucleotides at the polymorphic locus thereby determining a ratio of nucleotides at the polymorphic locus in the sample (page 11, lines 8-12 and Fig. 5).

Regarding Claim 33, Whitcombe et al disclose the method wherein the ratio of nucleotides at two or more polymorphic loci are determined simultaneously i.e. multiplex (page 8, lines 7-9).

Regarding Claim 35, Whitcombe et al disclose the method wherein two or more regions of DNA each of which comprise a polymorphic locus are amplified in a single reaction mixture (page 7, lines 11-15).

4. Claims 3 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (WO 97/42345, published 13 November 1997) in view of Lane et al (U.S. Patent No. 6,165,714, filed 16 December 1997) as applied to Claims 1 and 23 above and further in view of Hames et al. (Nucleic Acid Hybridization: a practical approach, 1988, pages 35, 36 and 42-44)

Regarding Claims 3 and 25, Whitcombe et al teach the methods of Claim 1 & 23 comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (tag region) which is identical in sequence to all or part of a probe on a solid support (capture

probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to al or part of the probe; labeling the amplified DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support wherein the presence of said labeled amplified DNA products on the solid support indicates that the nucleic acid sample contains at the polymorphic locus a nucleotide which is the same as the 3' terminal nucleotide of the primer (page 1, line 28-page 3, line 6, Fig. 13(b) and Claims 1 & 8). The first primer of Whitcombe et al comprises a capture region and terminates at the 5' end with a tag sequence for identification of the amplified product (page 14, lines 6-9) but they do not teach the first primer terminates at the 5 'end with the capture region. However, Lane et al teach the similar method wherein a region of DNA is amplified using a primer pair wherein the first primer terminates at the 5' end with a portion which is identical to the probe on the solid support (Column 8, lines 36-40 and Fig. 9B #80). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the tag-comprising primer of Whitcombe et al by terminating the primer at the 5' end with the capture sequence as taught by Lane et al to thereby simplify primer design by elimination of the tag sequence. Lane et al teach that the extension product is detected upon capture (Column 8, lines 23-41). Therefore, the tag sequence of Whitcombe et al is not required for extension product detection. Hence, one of ordinary skill in the art would have been motivated to eliminate the tag sequence of the Whitcombe et al primer based on the teaching of Lane et al wherein the tag sequence is not required for product detection.

Whitcombe et al teach the step of labeling couples a labeled nucleotide to a 3' end i.e. labeled NTPs are incorporated into the primer extension products by coupling to the 3' end

during primer extension (page 3, lines 5-6) but they do not teach a terminal transferase catalyzes the step of labeling. However, it was known in the art that terminal transferase labels a 3' end specifically (see Hames et al. page 35-36). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the labeling of Whitcombe et al. with the terminal transferase catalyzed labeling taught by Hames et al. for the known benefits of terminal transferase specificity as taught by Hames et al. (page 36, first full paragraph).

5. Claims 5, 14-16, 27 and 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (WO 97/42345, published 13 November 1997) in view of Lane et al (U.S. Patent No. 6,165,714, filed 16 December 1997) as applied to Claims 1 and 23 above and further in view of Harris et al (WO 94/02634, published 3 February 1994).

Regarding Claims 5 and 27, Whitcombe et al teach the method to determine a nucleotide at a polymorphic locus in a nucleic acid sample (page 5, lines 11-30). The method comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (tag region) which is identical in sequence to all or part of a probe on a solid support (capture probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to al or part of the probe; labeling the amplified

DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support wherein the presence of said labeled amplified DNA products on the solid support indicates that the nucleic acid sample contains at the polymorphic locus a nucleotide which is the same as the 3' terminal nucleotide of the primer (page 1, line 28-page 3, line 6, Fig. 13(b) and Claims 1 & 8) wherein the label is fluorescent (Claim 5) or enzymatic (page 14, lines 10-15) but they do not teach the label is radioactive. However radioactive labels were well known in the art at the time the claimed invention was made as taught by Harris et al. Harris et al teach a similar method of determining a nucleotide at a polymorphic locus (page 36, 2. through page 37 3.). The method comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to all or part of the probe; and hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support (Claim 1) wherein the label is selected from the group consisting of fluorescence, enzymatic and radioactive (Claim 14). Therefore, Harris et al teach the fluorescent, enzymatic and radioactive labels are functional equivalents. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the fluorescent and/or enzymatic label of Whitcombe et al with the functionally equivalent radioactive label as taught by Harris et al because one of ordinary skill would have expected the radioactive label to function in an manner equivalent to that of fluorescent and enzymatic labels.

The courts have stated with regard to chemical homologs that the greater the physical and chemical similarities between the claimed species and any species disclosed in the prior art, the greater the expectation that the claimed subject matter will function in an equivalent manner (see *Dillon*, 99 F.2d at 696, 16 USPQ2d at 1904).

Regarding Claims 14-16 and 36-38, Whitcombe et al teach the method wherein the probe is immobilized on a solid support (page 2, line 31-page 3, line 2) but they are silent regarding the composition of the solid support. Harris et al teach the similar method wherein the solid support is selected from the group consisting of beads (as recited in instant Claims 14 & 36); microtiter dish (as recited in instant Claims 15 & 37); a high density array (as recited in instant Claims 16 & 38 and defined on page 12, lines 2-5 of the specification i.e. for detecting more than 10 targets). Harris et al teaches these solid supports wherein their microtiter trays detect more than 10 targets and therefore meet the limitations of the instantly claimed high density array (page 11, first full paragraph-page 12, third paragraph). Harris et al also teach a motivation for utilizing their solid supports i.e. provide for high volume diagnostic applications (page 12, third paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solid supports of Harris et al to the method of Whitcombe et al wherein the multiplex capture probes are immobilized on a solid support for the expected benefit of providing high volume diagnostic applications as taught by Harris et al (page 12, third paragraph).

6. Claims 7 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (WO 97/42345, published 13 November 1997) in view of Lane et al (U.S. Patent No. 6,165,714, filed 16 December 1997) as applied to Claims 1 and 23 above and further in view of Vary et al. (U.S. Patent No. 4,851,331, filed 16 May 1986)

Regarding Claims 7 & 29, Whitcombe et al teach the methods of Claims 1 and 23 comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (tag region) which is identical in sequence to all or part of a probe on a solid support (capture probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to al or part of the probe; labeling the amplified DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support wherein the presence of said labeled amplified DNA products on the solid support indicates that the nucleic acid sample contains at the polymorphic locus a nucleotide which is the same as the 3' terminal nucleotide of the primer (page 1, line 28-page 3, line 6, Fig. 13(b) and Claims 1 & 8) wherein the nucleotide is indirectly labeled (page 3, lines 2-3) which suggests the nucleotide is epitope-labeled for antibody detection but they do not specifically teach epitopically labeled. Furthermore, Vary et al teach a similar method comprising: amplifying a region of DNA comprising the polymorphic locus; labeling the amplified DNA to form labeled amplified DNA products; and hybridizing the labeled DNA products to the probe on a solid support (Column 7, lines 43-49 and Fig. 3 A and B) and optionally detecting the labeled DNA products hybridized to the probe on the solid

support to thereby detect a nucleic acid containing a polymorphic locus (Column 4, lines 53-56) wherein labeling couples a labeled nucleotide to a 3' end (Column 3, lines 54-61). Lane et al. teach a similar method to determine a nucleotide analyte comprising: amplifying a region of DNA comprising using a primer pair, wherein the first primer comprises a 3' portion which is complementary to the region of DNA and a 5' portion which is identical to a portion of a probe on a solid support and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to all or part of the probe; hybridizing the amplified products to the probe on the support such that the second strand hybridizes to the support; and detecting the amplified products wherein the presence of amplified products indicates the nucleic acid sample contains the nucleotide analyte (Column 8, lines 36-41 and 9B) wherein the nucleotide is epitopically labeled for antibody-detection (Column 3, lines 63-65 and Column 4, line 66-Column 5, line2).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the fluorescent and/or enzymatic label of Whitcombe et al with a functionally equivalent epitopic label as taught by Vary et al because one of ordinary skill would have expected the epitopic label to function in an manner equivalent to that of fluorescent and enzymatic labels based on the teaching of Vary et al (Column 3, lines 63-65 and Column 4, line 66-Column 5, line2).

7. Claims 12 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al (WO 97/42345, published 13 November 1997) in view of Lane et al (U.S. Patent No. 6,165,714, filed 16 December 1997) as applied to Claims 1 and 23 above and further in view of Brown et al (U.S. Patent No. 5,807,522, filed 7 June 1995).

Regarding Claims 12 and 34, Whitcombe et al teach the methods of Claims 1 and 23 comprising: amplifying a region of DNA comprising a polymorphic locus in the sample to form amplified DNA product using a primer pair wherein a first primer (diagnostic primer) terminates at its 3' end at the polymorphic locus wherein the first primer comprises a 3' portion (detector region) which is complementary to the region of DNA and a 5' portion (tag region) which is identical in sequence to all or part of a probe on a solid support (capture probe) and not complementary to the region of DNA to form a first strand and a second strand wherein the first strand comprises a portion identical to all or part of the probe and the second strand comprises a 5' portion complementary to al or part of the probe; labeling the amplified DNA products for form labeled amplified DNA product (via a detector species); hybridizing the labeled amplified DNA product hybridized to the probe on the solid support such that the second strand hybridized to the probe on the solid support; and detecting labeled amplified DNA products hybridized to the probe on the solid support wherein the presence of said labeled amplified DNA products on the solid support indicates that the nucleic acid sample contains at the polymorphic locus a nucleotide which is the same as the 3' terminal nucleotide of the primer (page 1, line 28-page 3, line 6, Fig. 13(b) and Claims 1 & 8) wherein the method assays multiple are performed (i.e. multiplex ARMS) wherein individual assays of the multiplex assay work with similar efficiency (page 8, lines 7-9) which clearly suggests that the samples comprise DNA from two or more individuals, but they do not specifically teach two or more individuals. However, multiplex reactions comprising DNA from two or more individuals were well known in the art at the time the claimed invention was made as taught by Brown et al (Column 15, lines 19-22 and 59-61). It would have been obvious to one of ordinary skill in the

art at the time the claimed invention was made to apply the multiplex assay wherein samples comprising DNA from two or more individuals are analyzed simultaneously as taught Brown et al to the multiplex assay of Whitcombe et al based on the suggestion of Whitcombe (page 8, lines 7-9) for the expected benefit of rapid and convenient diagnostic analysis of multiple individuals as taught by Brown et al (Column 15, lines 19-22 and 59-61).

Response to Arguments

8. Applicant's arguments have been thoroughly reviewed and considered. However, the arguments are deemed moot in view of the fact that the argument address the previous rejection which have been withdrawn in view of the amendments and new grounds for rejection discussed above.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
June 24, 2003